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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,857	12/05/2006	Satoshi Inouye	09707.0008	4650

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EXAMINER	
HAQ, SHAFIQUL	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,857	INOUYE, SATOSHI	
	Examiner	Art Unit	
	SHAFIQUL HAQ	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-56* is/are pending in the application.

4a) Of the above claim(s) *3-5,10-12 and 18-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-9 and 13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/5/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election-Restriction

1. Applicants' election without traverse of Group I, claims 1, 2, 6-16, 17 and 29 drawn to fluorescent protein having a chemiluminescent activity, filed 27 March 2009 in response to Office Action dated 01 January 2009, is acknowledged and entered. Claim 29 was erroneously included in Group I, which should be in Group VII only (see Group VII, which includes claims 29 and 31) and therefore, claim 29 is removed from Group I invention.

   Applicants' election of "apoaequorin" for "apoprotein", "coelenteramid" as disclosed by the structure in upper left on page 33, "coelenterazine" as disclosed by the structure in upper right on page 33 and "calcium ion" for an ion that can be substituted for calcium ion is also acknowledged. Claims 10-12 of the elected group do not read on the elected species.

   Because applicant did not traverse the restriction requirement, the restriction requirement is deemed proper and is made FINAL.

   Therefore, claims 3-5, 10-12, 18-56 are withdrawn from further consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Applicants preserve their right to file a divisional on the non-elected subject matter.

2. Claims 1 and 2 are cancelled by Applicants and therefore, claims 6-9 and 13-17 are examined on merits in this office action.

Specification

3. Applicants' amendment to specification to replace the title with "FLUORESCENT PROTEIN" is acknowledged and entered.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 recites "wherein the calcium ion or the divalent or trivalent ion that can be substituted for the calcium ion is on selected from the group consisting of a calcium ion , a strontium ion and a lead ion". The claim is confusing as to what is intended to encomass by "substituted for the calcium ion" by "a calcium ion"?

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 6, 7, 8, 9, 13, 14, 15, 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Kurose *et al* (PNAS 1989).

Claim 6 is directed to a composition comprising an apoprotein that is a component of a calcium-binding photoprotein, a coelenteramid or an analog thereof, and a calcium ion or a divalent or trivalent ion that can be substituted for the calcium ion. The recitation "a fluorescent protein having a chemiluminescent activity" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. Applicant is reminded that a recitation of the intended use of the claimed invention, i.e. “fluorescent protein having a chemiluminescent activity”, must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963).

With regard to claim 6, Kurose *et al* disclose a fluorescent protein (bFP) having chemiluminescence activity comprising apoaequorin, coelenteramide and calcium ion (page 80, lines 4-16 of left column).

With regard to claim 7, Kurose *et al* teach that the photoprotein consists of two components: an apoprotein (apoaequorin) and a chromophore and the chromophore is made up of coelenterazine and molecular oxygen. Kurose *et al* further teach that aequorin contains three Ca^{2+} binding sites and binding of calcium to these sites induces a conformational change in the protein, causing an active site to be formed, which caralyzes the oxidation of the bound coelenterazine to coelenteramide (page 80, lines 4-16 of left column), which thus teaches a complex of apoaequorin with a coelenteramide (1:1) and upto three calcium ions bound to the complex as there are three Ca^{2+} binding sites (i.e. 1:3).

With regard to claim 8, Kurose *et al* teach apoaequorin as apoprotein .

With regard to claim 9, the amino acid sequence of SEQ ID NO:1 is an amino acid sequence for apoaequorin from jellyfish *Aequorea Victoria* and the sequence is inherently present in the apoaequorin as disclosed by Kurose *et al* because Kurose *et al* teach apoprotein of jellyfish *Aequorea Victoria.*

With regard to claim 13, Kurose *et al* teach fluorescent protein mutant having chemiluminescence activity comprising mutant apoaequorin wherein at least one of at least two free sulfhydryl group is mutated to serine to disrupt disulfide bonds (see Table 1), coelenteramide and calcium ion (see "RESULTS" section of pages 81-82 and page 83, lines 22-25 of left column).

With regard to claims 14 and 15, Kurose *et al*, as described above, disclose fluorescent protein (bFP) having chemiluminescence activity comprising apoaequorin, coelenteramide and calcium ion (page 80, lines 4-16 of left column) and the coelenteramide reads on the compound of formula (1), when X^2=H, X^1=OH, R^3=H, R^1=an arylated alkyl group substituted with hydroxyl group and R^2=an unsubstituted arylated alkyl group and with regard to claim 17, the compound reads of coelenteramid when R^1= p-hydroxybenzyl group and R^2= benzyl group.

With regard to claim 17, Kurose *et al* teach binding of calcium ion to aequorin, which triggers oxidation of coelenterazine to coelenteramide (page 80, lines 4-16 of left column).

8. Claims 6, 8, 9, 14, 15, 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Inouye *et al* (FEBS Letters 1994).

Claim 6 is directed to a composition comprising an apoprotein that is a component of a calcium-binding photoprotein, a coelenteramid or an analog thereof, and a calcium ion or a divalent or trivalent ion that can be substituted for the calcium ion. The recitation "a fluorescent protein having a chemiluminescent activity" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. Applicant is reminded that a recitation of the intended use of the claimed invention, i.e. “fluorescent protein having a chemiluminescent activity”, must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963).

Inouye *et al* teach that binding of Ca^{2+} to aequorin triggers intramolecular reaction in which coelenterazine is oxidized to coelenteramide, yielding as products a blue fluorescent protein blue wherein the coelenteramide is bound to apoaequorin (page 277, lines 9-21 of left column). Therefore, blue fluorescent protein (bFP) comprises Ca^{2+}, apoaequorin and coelenteramide and the blue fluorescent protein

as being having the same composition as the claimed invention would be expected to have chemiluminescent activity. In fact, Inouye *et al* teach that the bFP produces chemiluminescence in the presence of GFP.

With regard to claim 8, Inouye *et al* teach apoaequorin as apoprotein (page 277, lines 4-5 of left column)..

With regard to claim 9, the amino acid sequence of SEQ ID NO:1 is an amino acid sequence for apoaequorin from jellyfish *Aequorea Victoria* and the sequence is inherently present in the apoaequorin as disclosed by Inouye *et al* because Inouye *et al* teach apoprotein of jellyfish *Aequorea Victoria.*

With regard to claims 14 and 15, Inouye *et al*, as described above, disclose fluorescent protein (bFP) having chemiluminescence activity comprising apoaequorin, coelenteramide and calcium ion (page 277, lines 9-21 of left column) and the coelenteramide reads on the compound of formula (1), when X^2=H, X^1=OH, R^3=H, R^1=an arylated alkyl group substituted with hydroxyl group and R^2=an unsubstituted arylated alkyl group and with regard to claim 17, the compound reads of coelenteramid when R^1= p-hydroxybenzyl group and R^2= benzyl group.

With regard to claim 17, Inouye *et al* teach binding of calcium ion to aequorin, which triggers oxidation of coelenterazine to coelenteramide (page 80, lines 4-16 of left column).

9. Claims 6, 8, 9, 14, 15, 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Kojima *et al* (Tetrahedron Letters 1997).

Claim 6 is directed to a composition comprising an apoprotein that is a component of a calcium-binding photoprotein, a coelenteramid or an analog thereof, and a calcium ion or a divalent or trivalent ion that can be substituted for the calcium ion. The recitation "a fluorescent protein having a chemiluminescent activity" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. Applicant is reminded that a recitation of the intended use of the claimed invention, i.e. “fluorescent protein having a chemiluminescent activity”, must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963).

Kojima *et al* teach that binding of Ca^{2+} to aequorin triggers intramolecular reaction in which coelenterazine is oxidized to coelenteramide, yielding as products a blue fluorescent protein blue wherein the coelenteramide is bound to apoaequorin (page 2875 and lines 1-5 on page 2876). Therefore, blue fluorescent protein (bFP) comprises Ca^{2+}, apoaequorin and coelenteramide and the blue fluorescent protein

as being having the same composition as the claimed invention would be expected to have chemiluminescent activity. In fact, Kojima *et al* teach that the bFP produces chemiluminescence in the presence of GFP (lines 3-5 on page 2876).

With regard to claim 8, Kojima *et al* teach apoaequorin as apoprotein (page 2875, line 4).

With regard to claim 9, the amino acid sequence of SEQ ID NO:1 is an amino acid sequence for apoaequorin from jellyfish *Aequorea Victoria* and the sequence is inherently present in the apoaequorin as disclosed by Kojima *et al* because Kojima *et al* teach apoprotein of jellyfish *Aequorea Victoria.*

With regard to claims 14 and 15, Kojima *et al*, as described above, disclose fluorescent protein (bFP) having chemiluminescence activity comprising apoaequorin, coelenteramide and calcium ion (page 2875 and lines 1-5 on page 2876) and the structure of coelenteramide (see compound 2 of Scheme 1) reads on the compound of formula (1), when X^2=H, X^1=OH, R^3=H, R^1=an arylated alkyl group substituted with hydroxyl group and R^2=an unsubstituted arylated alkyl group and with regard to claim 17, the compound reads of coelenteramid when R^1= p-hydroxybenzyl group and R^2= benzyl group.

With regard to claim 17, Kojima *et al* teach binding of calcium ion to aequorin, which triggers oxidation of coelenterazine to coelenteramide (Lines 1-5 on page 2876).

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 6-9 and 14-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3-8 of U.S. Patent No. 7,396655. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the instant claims (i.e. a composition comprising an apoprotein that is a component of a calcium-binding photoprotein, a coelenteramid or an analog thereof, and a calcium ion or a divalent or trivalent ion that can be substituted for the calcium ion) are fully disclosed in cited claims of US paten '655. As for example, claim 3 of US patent '655 discloses a fluorescent protein comprising an apoprotein of a calcium-binding photoprotein, a coelenteramide or an analog thereof, and a calcium ion or a divalent or trivalent ion that can be substituted for calcium ion and claim 3 also recites proportion of apoprotein, coelenteramide and calcium ion in the composition, which reads on the

subject matter of claim 7 of instant application. As for claims 8-9 of instant application, the limitations are taught in claims 4-5 of US patent '655 and as for claims 14-17, the limitations are taught in claims 6-8 of the US patent '655 .

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shafiqul Haq/
Primary Examiner, Art Unit 1641